Transplantation of Gene-Corrected Autologous CD34+ Hematopoietic Stem Cells in Previously Transplanted Patients with JAK3 Deficiency and Persistent Humoral Immune Defects

PIs: Sorrentino, Cunningham, and Buckley

SCIENTIFIC ABSTRACT

Deficiency of Janus Kinase 3 (JAK3) is a rare cause of severe combined immunodeficiency (SCID) in humans. The standard treatment for this disorder is allogeneic stem cell transplantation, either using a matched sibling or one of the child's parents as a donor for normal stem cells. Transplantation usually results in reconstitution with normal donor-derived T-cells. However, B-cell function often remains defective, resulting in the need for long-term treatment with intravenous gamma-globulin. The goal of this protocol is to test the safety of a gene therapy strategy designed to restore autologous B-cell function in patients with JAK3-deficient SCID. To achieve this objective, we plan to harvest hematopoietic stem cells from patients with proven JAK3 deficiency, who have previously undergone allogeneic transplantation but have persistent humoral immunodeficiency. Purified $CD34^+$ cells derived from this graft will be transduced with a JAK3-expressing retroviral vector. These cells will be infused into unablated patients to determine the toxicity of this treatment and to evaluate the ability of these cells to reconstitute normal B-cell function.